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## Neurophysiological Basis of Rehabilitation Technology

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**DOI**
10.1007/978-3-031-08995-4_3

**Publication date**
2022

**Document Version**
Final published version

**Published in**
Neurorehabilitation Technology, Third Edition

# 3 Recovery of Sensorimotor Functions After Stroke and SCI: Neurophysiological Basis of Rehabilitation Technology

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**Abstract**

After a stroke or spinal cord injury (SCI), there exists an inherent individual capacity for recovery of function that depends on factors such as location and severity of central nervous system (CNS) damage. This capacity can be determined early after the incident by clinical, electrophysiological, and imaging examinations. These measures can also be used as prognostic factors and, consequently, for an early selection of appropriate rehabilitation procedures. Recovery of function after a stroke mainly depends on the tract damaged and the amount of damage, e.g., recovery of hand/finger function is particularly poor after extensive lesioning of the corticospinal tract. In cervical SCI, the combination of peripheral and central nervous system damage limits recovery. As the recovery of function usually remains incomplete, an integral part of rehabilitation should be directed to compensate for the remaining motor deficit by customized assistive devices that promote independence in daily life activities. The capacity for the recovery of function can be exploited by a repetitive execution of functional movements, physically supported as far as required. This approach encourages participation by the patient and promotes appropriate proprioceptive input from limb muscles, tendons, skin, and joints under physiological movement conditions. The consequence of this knowledge is that robotic assistance has to be adapted to the actual condition and requirements of the individual patient. Furthermore, intensive training (i.e., a high number of movement repetitions and long training duration) can lead to an additional gain in function compared to low-dose conventional training. However, this gain is small compared to the spontaneous recovery of function and is often transient, due to the fact that patients will not regularly use these functions in daily life, thereby maintaining them. Finally, other promising adjuvant approaches could contribute to improving motor function in the future, such as epidural or deep brain stimulation as well as CNS repair. However, they are still in an early clinical or in a translational stage.

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D. J. Reinkensmeyer et al. (eds.), *Neurorehabilitation Technology*,
https://doi.org/10.1007/978-3-031-08995-4_3

**Keywords**

Neurophysiology · Stroke · Spinal cord injury (SCI) · Recovery of function · Rehabilitation technology

## 3.1 Introduction

The aim of neurorehabilitation is to improve function after damage to the nervous system. This chapter focuses on the neurophysiological aspects that determine the recovery of function after stroke and SCI. Our premise is that insights into these neurophysiological aspects should influence the design of rehabilitation technologies, such as robotic devices, that are to be applied in neurorehabilitation. We specifically seek to address the following questions: What are the limits of the recovery of function? And, taking into account these limits: What are the neurophysiological aspects that can be leveraged to optimize the effectiveness of neurorehabilitation approaches for restoring upper and lower limb function in stroke and SCI? Based on the answer to these questions, we propose the following principles for promoting recovery: (1) Where the potential for biological recovery is substantially limited, relevant aspects of the residual neurophysiology should be leveraged to promote compensation; (2) Where the potential for biological recovery is high, limb muscle activation and proprioceptive input should be promoted as much as possible in a physiological manner during training to promote restoration of function; and (3) Sufficient dosage of physiologically appropriate training should be delivered to overcome an apparently nonlinear dose–response relationship. We discuss the implications of these principles for the design of rehabilitation technology.

1. Where the potential for biological recovery is limited, residual neural circuits should be leveraged.

There are fundamental constraints to recovery after stroke and SCI [1]. Much of the recovery of function in stroke [2] and SCI [3] during the first three months is due to resolving neurapraxia that occurs in parallel to the smaller effects of the rehabilitative treatments that exploit neuroplasticity [4]. For example, after stroke, most patients reach a seeming plateau after recovering approximately 70–80% of the initial proximal arm muscle function impairment [5–7].

The severity and localization of the CNS damage determine the specific range of an individual patient's achievable function, independently of the rehabilitation training [8, 9]. For example, after brain damage that includes substantial lesions of pyramidal tract connections to hands and fingers, the motor deficit can only partially be compensated by the activation of other non-damaged tracts/brain areas. Such compensation typically only restores gross hand flexion but not individual finger dexterity [5, 6, 10]. Consequently, substantial damage to the pyramidal tract means that only modest recovery of hand and finger function can usually be expected [7, 11] (Fig. 3.1a). In contrast, a more favorable recovery of upper extremity function can be expected following damage to other brain areas [5, 6, 10].

Similarly, after spinal cord damage, the improvement of upper limb function depends on the level and extent of the lesion [3]. In cervical cord injuries, a combined damage to the central (spinal tracts) and peripheral nerval structures (motoneurons and roots to arm, hand, and finger muscles) occurs. This results in an arm/hand/finger paresis associated with a mixture of spastic and flaccid muscle tone [12]. The peripheral part of nervous system damage can account for up to 50% of paresis [13] which has little potential to recover. After a sensorimotor complete cervical SCI, functionally meaningful recovery of upper extremity function cannot occur [14] (Fig. 3.1a).

Demographic and sociological factors may limit recovery as well. For example, while the age of patients has little influence on the recovery of the neurological deficit post-stroke [17] and SCI [18], a young person with a SCI can better translate the recovery of motor system deficits into movement capabilities that support daily life activities compared to elderly subjects [18].

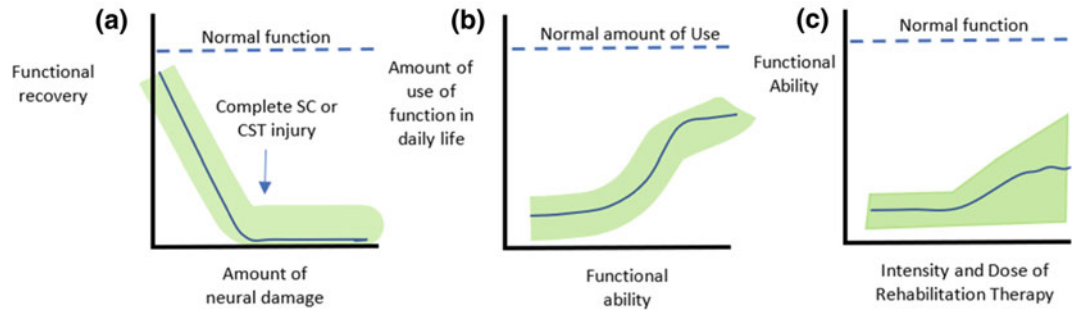


**Fig. 3.1** Nonlinear relationships in neurorehabilitation recovery. **a** The amount of functional recovery that can be expected declines with more severe neuroanatomical damage, with a complete injury to the spinal cord (SC) or corticospinal tract (CST) profoundly limiting functional recovery. The green band denotes the variability in this relationship due to a range of factors, including the location of the damage, patient demographics, and intensity of rehabilitation. **b** Another nonlinearity describes the *usefulness to the patient* of any recovered functional movement ability. A patient will not regularly use a function throughout the day (such as hand grasp or walking) if the functional ability does not exceed a threshold. This graph is based on figures in [15, 16]. The green band again denotes a relatively high variability across patients. **c** The relationship of functional ability to the intensity and dose of rehabilitation may also be nonlinear, requiring a relatively high threshold of therapy to be achieved before a dose–response relationship can be identified, compared to what is usually delivered in clinical and research settings. Again, the green band denotes the effect of rehabilitation depends on other factors, including lesion location and size, patient demographics, and timing of therapy

Finally, it is important to note that moderate recovery of movement ability may not always be useful to patients. For example, a recent study used a magnetic, wearable finger movement sensor to quantify the movement of the fingers and wrist in daily life after a stroke [15]. It was observed that people with a stroke must recover a substantial amount of hand function (~50% of normal hand function as measured on the Box and Blocks Test), in order to begin to actually use their paretic hand in the home environment. This is consistent with the "Threshold Hypothesis" proposed by Schweighofer et al. [19]. Thus, even substantial recovery of hand function can have limited pragmatic usefulness to a patient in daily life (Fig. 3.2b). A similar phenomenon has been observed for walking after stroke, where individuals with a score up to 50% normal on the Berg Balance Scale had low daily walking amounts, as measured with a wearable sensor [16]. Furthermore, after a SCI, a threshold of force recovery of leg muscles (i.e., lower extremity motor score) is required for the performance of stepping movements [20]. Nevertheless, the "threshold" of usefulness might be dependent on the potential use of compensatory strategies and assistive technologies, e.g., during locomotion in SCI subjects.

For functions where severe anatomical damage limits recovery, the guiding principle is to leverage the relevant changes in the sensorimotor nervous system. For example, spasticity can contribute to the compensation of movement deficits [21–23], thereby contributing to the restoration of function. After a stroke or an incomplete SCI, a loss of supraspinal drive leads to limb paresis. Concerning lower limb function, the inability to perform stepping movements due to muscle paresis leads to reduced mobility. However, with the development of spastic muscle tone, the stiff leg can support the body during stance, i.e., the deficit becomes partially compensated. Functional movements, such as stepping, can be executed on a lower level of muscle tone regulation, i.e., the contribution of spastic muscle tone to support the body during movement performance [24]. Therefore, most post-stroke subjects can regain walking function by using the spastic-paretic leg more or less stick-like supporting the body in the stance phase and

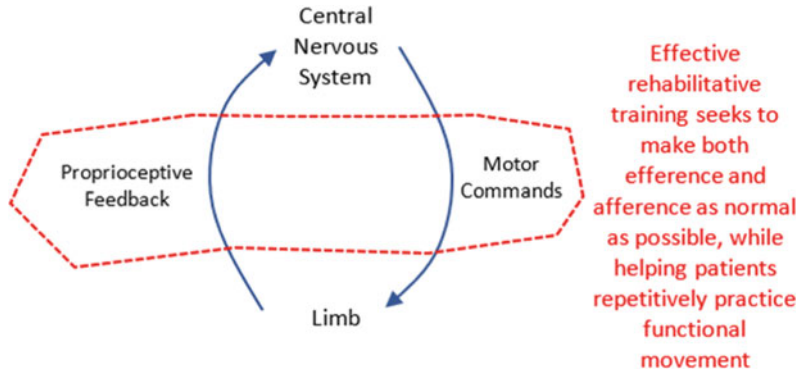


**Fig. 3.2** Conceptual approach to optimizing return of function through use-dependent plasticity mechanisms. The improvement of function within the residual capacity depends on the appropriate activation of motoneuron pools and proprioceptive sensors of limb muscles under physiological movement conditions

circumducting the leg during swing (due to reduced knee flexion). However, the normal push-off at the end of the stance phase is lost. Over time, little change in biomechanical and muscle activation characteristics of the spastic-paretic leg takes place [14, 25]. In this scenario, the limited improvement of walking ability achieved over the course of rehabilitation after a stroke is due to adaptational changes (compensation) rather than due to a restoration of the "normal" stepping function.

Concerning upper limb function, early after stroke, flaccid arm muscle paresis prevails, i.e., the limbs are weak and do not resist passive displacement. In the weeks following stroke, spastic muscle tone usually becomes more pronounced in the wrist and finger flexors than in the extensor muscles, as the antigravity muscles have more muscle mass [24, 26]. Thus, with the development of some spastic muscle tone, rudimentary grips can be performed and the training of residual muscle function can be initiated [14]. In this stage, the focus of training should be directed to enable the execution of simple reach and grasp functional tasks, as well as self-care movements. Patients suffering a cervical SCI (e.g., C6/7) or severe stroke can make use of spastic muscle tone to perform simple grasp movement (the so-called tenodesis grasp). Furthermore, spastic proximal arm muscles can provide some passive gravity support to carry an object from one to another spot.

The pragmatic goal of rehabilitation therapists is not primarily to re-establish "normal" movement performance, but usually focuses on enabling compensatory movement control, which typically involves "simpler", less well-organized movements that help maximize independence during activities of daily living (ADL) for the individual patient [27]. As we have described, this may be aided by changes in muscle mechanical properties related to spastic muscle tone that develops during the spontaneous recovery of function [23]. Thus, a therapist may choose to focus on learning to use abnormal motor control and biomechanics for the performance of activities of daily living or to bypass physiological function with assistive technology (e.g., a wheelchair), rather than on restoring normal muscle control. However, it is important to note that, while the compensatory approach may enable the patient to perform needed upper and lower limb functions to regain independence, it may also establish a "local minimum" of recovery that is less than the theoretical maximum possible, specifically in cases where neuroanatomical resources for neuroplasticity and motor learning are available but not utilized.

2. Where the potential for recovery is high, limb muscle activation and proprioceptive input should be promoted in a physiological way during training.

When sufficient neuroanatomical resources remain, relearning of physiological movements can be optimized by encouraging limb muscle activation and by providing appropriate proprioceptive input to the spinal and supraspinal neural centers with the goal to activate preserved neural circuits in as normal a way as possible (Fig. 3.2). Within this framework, the level of physiological limb muscle activation and normal proprioceptive information serves as a marker for predicting the achievement of training effects.

We begin with the lower extremity. In the early nineties, functional locomotor training with body-weight unloading of para- and tetraparetic SCI subjects was introduced. This was based on the observation that key aspects of locomotor function in cat SCI models recover quite well during treadmill training with body-weight unloading (BWSSTT) [28].

In severely paralyzed patients due to an SCI, automatic stepping movements can be induced, associated with a physiological leg muscle activation (i.e., close-to-normal timing of electromyography [EMG] patterns with smaller than normal amplitude), when patients stand on a moving treadmill with the body unloaded up to 80% [29, 30]. This leg muscle activation during the stance phase of gait is triggered by load receptor input from the ground reaction forces [31]. Furthermore, as observed in studies in cats [32], sufficient hip extension at the end of the stance phase is essential for the initiation of the swing phase and contribution to the generated EMG signal pattern during stepping [30]. The consequence is a physiological limb muscle activation induced by inputs from load and hip-joint-related proprioceptive receptors that represents the prerequisite for the improvement of locomotor function in rodents [33] and patients with a stroke or SCI (for review see [14]). With a gain of strength in the proximal leg muscles, body-weight unloading can then be reduced and self-induced stepping movements become possible. This is associated with an increase in the strength of leg muscle activation. Thus, during the course of training, body un-/reloading can be adapted to the subject's actual degree of paresis.

In completely paralyzed patients suffering an SCI who do not undergo functional locomotor training, such as body-weight-supported treadmill training (BWSTT), spinal neural circuits underlying stepping movements undergo degenerative changes associated with a loss of neural activity, i.e., neurons become silent even when appropriate proprioceptive input is provided. In the long term, the lack of locomotor training results in a neuronal dysfunction below the level of the lesion in both rodents [34] and patients with SCI [35].

In incompletely paralyzed SCI patients, BWSTT has been shown to result in a similar outcome of stepping function compared to a conventional rehabilitation provided by therapists approach. Nevertheless, BWSTT reduces the physical burden for the therapist [36]. Gait speed during locomotor training represents another factor that influences the locomotor ability outcome. In ambulatory stroke patients, a successive increase of treadmill speed through a physiological range up to 20% increase of initial speed during a 4-week training period results in a better walking ability than conventional gait training [37].

Most of the recovery of function occurs during the first three to four months after CNS damage. Nevertheless, some gain in gait velocity, endurance, and performance can be achieved by automated locomotor training with a driven gait orthosis in chronic patients with an incomplete SCI and stroke [38]. However, it should be noted that passively induced leg movements by rigid robotic assistance [39] during locomotor training results in reduced therapeutic efficacy [40]. Further improvement of locomotor function after damage to the CNS is associated with minor changes in the leg muscle activity pattern and relies on a better coordination between the legs and an adapted spastic muscle tone, as shown after stroke [25] and SCI [22].

Turning to the upper extremity, evidence for the importance of generating physiological limb muscle activation during training is less direct but the evidence is growing. For the lower extremity, as described above, physiological limb

activation can be seen as generating a set of necessary sensory pre-conditions for triggering and/or facilitating cyclic locomotor activity, which is then reinforced through repetitive practice. For the upper extremities, physiological limb movement activation appears to facilitate motor learning processes that contribute to the restoration of function.

Simply moving the passive upper limb is not sufficient to stimulate these learning processes. For example, no motor recovery was observed in chronic stroke patients when the paretic wrist was moved passively by a robotic therapy device for several hours per week over several weeks (except for small reductions in muscle tone) [41]. However, when the subjects were required to initiate wrist movements—measured with EMG—in order to receive movement assistance, recovery occurred. Thus, physiological self-activation of the upper limb muscles was a pre-condition for producing a training effect. A key neurophysiological mechanism that appears to be at play during passive training is "slacking", which is the algorithmic tendency of the motor system to reduce its effort and output when the kinematic error is small [42, 43].

A widely accepted approach to rehabilitate hand function after stroke is constraint-induced movement therapy (CIMT). This approach is based on the idea of enhancing recovery of function by reducing interhemispheric inhibition of the stroke hemisphere [44]. By immobilizing the non-affected hand, the patient is forced to use the paretic hand/arm for the performance of ADLs [45]. In an analysis of the Excite CIMT clinical trial, proprioceptive integrity was the strongest predictor of treatment effect from CIMT [46]. On average, patients suffering from impaired proprioception had a 20% probability of achieving a clinically meaningful outcome compared to those without clinically detected loss of proprioception.

A study of robotic-assisted finger training found that patients with impaired finger proprioception had a smaller functional benefit from robotic finger training compared to those with intact proprioception [7]. Proprioceptive integrity was quantified robotically at baseline by asking subjects to indicate when their index and middle fingers crossed each other as they were driven by a robotic exoskeleton. Proprioceptive error (i.e., the magnitude of the error in estimated finger-crossing angle) predicted 40% of the variance of the functional training effect. Further, neural injury to and abnormal activation of the somatosensory system were the strongest predictors of functional benefit from robotic hand therapy, chosen from an array of over 40 measures that included both motor and sensory variables related to anatomy, neurophysiology, and behavioral outcomes [47].

Other research increasingly implicates the importance of proprioception as a biomarker for predicting rehabilitation response of the upper extremity. For example, one study found that, for patients with chronic stroke, deficits in proprioception predicted motor learning associated with finger tracking training [48]. Clinical assessments of proprioception after stroke have shown value for predicting motor recovery [49, 50]. Lack of somatosensory evoked potentials early following stroke also predicts poor motor recovery [51, 52]. Theoretical models of recovery suggest that the reason that proprioception plays such a key role in predicting recovery is that accurate sensing of limb muscle force and movement is needed as a "teaching signal" to guide practice-driven changes in cortical activation patterns [53].

Finally, a common physiological mode of use of the upper extremities is bimanual control. Correspondingly, bilateral hand training for reaching and grasping tasks in stroke patients has been suggested to be more effective in improving unilateral execution of these tasks with the affected arm than unilateral training alone [54]. This might be a result of stronger recruitment of the contralesional hemisphere through bilateral compared to unilateral training [55]. Such bilateral hand movements, e.g., opening a bottle, are based on a task-specific control by a "neural coupling" of the hands. This is achieved either by a coupling of the hemispheres, i.e., both ipsi- and contralateral hemispheres become involved in bilateral hand movement tasks. Alternatively and more likely, each of the two hands becomes controlled by the cortico-reticulo-spinal tract

during the automatically performed cooperative hand movements [56] (cf. Chap. 6). Consequently, in post-stroke patients during the training of cooperative hand tasks, the unaffected hemisphere supports movements of the paretic hand and arm [57].

3. Dosage of training required to overcome a nonlinear dose–response relationship.

Several studies indicate that more intensive training—i.e., a high number of movement repetitions per hour (intensity) and long training duration (dose)—results in an additional gain in the upper and lower limbs function. This effect was reported for post-stroke subjects [58–65], as well as for subacute [66] and chronic [38] SCI subjects. By applying a very high dose of 300 h, clinically meaningful gains in arm/hand function were described in a chronic stroke population [67]. A positive effect of training intensity on the outcome of ambulation in stroke subjects [62] was also recently confirmed for subjects with SCI [66]. The intensity and dose of physical therapy were thought to have a positive effect on outcome in both animal [33] and human [68–70] studies. These observations suggest that the intensity provided in the standard of care, which is notably low (tens of movements per practice session over a limited number of sessions [17]), might not be sufficiently large enough. Timing of delivery of training may also be an important factor in establishing its effectiveness, with higher potential in the subacute window, as was recently shown for upper extremity rehabilitation after stroke [71].

Other studies have not found an effect of movement dose on functional recovery. Several studies of upper limb function of chronic post-stroke subjects found no evidence for a dose–response effect of training intensity on functional recovery [72, 17]. For lower limb function, the improvement of outcome achieved by a more intensive training was small and/or transient (cf. Fig. 3 of [73]) in relation to the gain in function achieved by a standard training in post-stroke [73] and SCI [66] subjects. In a large group (200 adults) of moderately to severely impaired subacute post-stroke subjects, a more intensive locomotor training was related to the improvement of stepping function. However, the BWSTT was not superior to relaxation sessions (of the same duration and in addition to standard therapy) in respect of walking speed and activities of daily living [74]. Finally, in incomplete SCI subjects, doubling the daily locomotor training time had only small effects on walking ability [66]. Therefore, questions concerning the additional gain of function achieved in relation to the spontaneous recovery of function, and whether this gain represents a lasting effect, remain open [9].

A reconciliation of these conflicting results may be possible if the dose–response relationship for movement training is nonlinear in nature (Fig. 3.1c). This has been suggested by a meta-analysis of experiments with a rodent model of upper extremity rehabilitation after ischemic stroke, which found that the dose–response relationship takes a curvilinear form [75]. This means that there is a range of levels of intensity for which changes in intensity have no effect on recovery. It may be that negative clinical trials have been in this range. Beyond this range, one might expect an increasing benefit from intensifying the training, which could account for the small cluster of successful high-dose studies. However, factors such as the neural tracts affected, the amount of damage, the level of SCI (e.g., cervical), the timing of rehabilitation, and the individual capacity for recovery are suggested to essentially determine the extent of functional recovery [9]. The appropriate range of training intensity and dose is expected to relate to the number of movements usually performed during daily life activities. Further, the neurophysiological mechanisms of this putative nonlinearity remain unclear and are an important topic for future study.

### 3.2 Implications for Rehabilitation Technology Design

Where the potential for recovery is limited due to the nature and extent of the anatomical damage, we have suggested that relevant aspects of the neurophysiology, such as abnormal muscle tone, should be leveraged. Several widely used non-actuated assistive devices are already based on this principle. Examples include wrist-driven tenodesis orthoses that support grip and ankle-foot orthoses that effectively further increase the tone of the ankle muscles to support walking. Several powered exoskeletons have also been developed to support overground walking (see review [76]) and hand/arm function [77, 78]). Determining how to best work with the relevant aspects of neurophysiology to maximize function is an important consideration for guiding future robotic design. We anticipate that compensatory movement strategies, strengthened with technological supports, will, for now, remain as important tools to mitigate motor deficits and promote independence [79].

When the potential for recovery is substantial due to sufficient anatomical resources, we have suggested that proprioceptive input and limb self-generated muscle activation should be promoted as much as possible in a physiological way during training to enhance the restoration of function. Special attention should be paid during the design of robotic therapy to prevent that the robot "over assists" the patient, as too much assistance might cause the patient to reduce the physiological contribution of efferents to training. One strategy is to provide limbs gravity support to allow patients to perform functional movements by their own (limited) effort [80]. Another strategy is to provide robotic assistance only following sensed self-initiated movement by the patient [81]. Another compatible approach is to keep the movement support provided by the therapist or device to a minimum in order to make the training optimally challenging and maximize the patient's contribution throughout the practiced movements (for reviews see [14, 81, 82]). An array of assist-as-needed algorithms have already been developed and can be used as resources in robotic therapy device design [81]. Conversely, error-augmentation algorithms that seek to amplify the movement error, promote movement variability (and thus, task exploration), and/or maximize patients' effort also exhibit potential [82–84].

Implementing such a variety of robotic training algorithms requires clever engineering design so that the device can achieve the wide range of impedances needed for these algorithms, ranging from complete mechanical transparency to full assistance. This has not yet been fully achieved for wearable and untethered robotics and remains a holy grail.

Physical interfaces and controllers should also be designed so as to minimize the alteration of sensory flow during training, taking into account the tactile stimulation the robot provides via its physical interface with the patient's limbs. Enhancing the congruency of sensory information—i.e., tactile, proprioception, vision, and auditory information—might not only enhance performance during training but also promote the transfer of the acquired skills during training to activities of daily living [85]. New technological developments, such as head-mounted displays and tactile actuators, could be incorporated into current robotic solutions to allow for a more naturalistic visualization of the patients' movements within the virtual environments [85, 86] and more realistic interactions with virtual tangible objects [87]. Finally, in the case where proprioception is impaired, robots can potentially play a key role in retraining proprioception. For example, with robotics, proprioceptive training can be gamified by using the robot to "display" game elements proprioceptively by driving the patient's limb [88]. Providing meaningful and easy-to-use tools to therapists for making an impact on proprioception could open novel avenues for treatment, given that accurate proprioception seems to serve as a gateway for motor learning as described above.

We described above the possibility that for some conditions (i.e., hand function) sufficient dosage of training must be delivered to overcome

an apparently nonlinear dose–response relationship. The introduction of rehabilitation robots was based on the widely accepted assumption that the recovery of function depends on the intensity of training. It now seems that this assumption may be correct only for a specific range of dose of training, i.e., there must be a sufficient dose, and the threshold dose is relatively high compared to standard clinical practice. Thus, studies of robotic therapy may have suffered from providing too low training dose, an ironic situation given that robotic therapy devices were specifically developed to allow longer training times and more repetitions. In many cases, then, the failure of a robot therapy device to prove useful may not be with the robot itself, but in the way it was applied —that is, it simply wasn't applied enough! Research is required on the institutional, structural, and pragmatic factors that limit the rehabilitation therapy dose that is typically achieved with or without rehabilitation technology.

Nevertheless, robot-assisted therapy can provide a number of other advantages besides increasing therapy dose, including a standardized training environment, adaptable support to the patient's specific needs, automatic monitoring of functional measures, and reduction of the physical burden on therapists. Rehabilitation robots are thus an ideal means to complement conventional therapy in rehabilitation centers if they are designed and applied on the basis of neurophysiological insights underlying the recovery of sensorimotor functions, as we have outlined.

## 3.3 Conclusion

It is concluded that there is an inherent and relatively fixed individual capacity for recovery of function after a stroke or SCI that depends on factors such as location and severity of CNS damage. This capacity can be determined early after CNS damage by clinical, electrophysiological [14], and imaging [5] examinations. These measures can also be used as prognostic factors and, consequently, for the selection of appropriate rehabilitation procedures early after CNS damage. Recovery of function after a stroke or SCI usually remains incomplete. Therefore, an integral part of rehabilitation should be directed to compensate for the remaining motor deficit by refined assistive devices that promote independence by working with the relevant aspects of residual physiology where possible.

The individual capacity for recovery of function, where it exists in a sufficient amount, can be exploited by a repetitive execution of functional movements, supported as far as required. The improvement of function within this capacity depends on the appropriate activation of descending systems as well as motoneuron pools by the input from proprioceptive sensors of limb muscles, tendons, skin, and joints under physiological movement conditions. The consequence of this knowledge is that robotic assistance has to be adapted to the actual condition and requirements of the individual patient, in such a way as to promote normal efferent and afferent physiological activation. Finally, a more intensive training can lead to an additional gain in function in relation to a standard training, if this training dose exceeds a specific threshold, although this gain is sometimes transient.

Finally, adjuvant approaches might help restore motor function in the future, such as epidural [89] or deep brain [90] stimulation as well as CNS repair, but they are still in an early clinical or in a translational stage. Their success will also likely depend on the generation of physiological patterns of limb muscle activation.

**Acknowledgements** DJR supported by NIH grant R01HD062744.

**Disclosure** David Reinkensmeyer has a financial interest in Hocoma AG and Flint Rehabilitation devices, makers of rehabilitation equipment. The terms of these arrangements have been reviewed and approved by the University of California, Irvine, in accordance with its conflict of interest policies.

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